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The association of diabetes and obesity with severity of dengue fever: An immunopathology update

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***Abstract*---**The arboviral infection dengue represents a global public health risk as the frequency of cases climbs across period and is anticipated to do so in the future. The fundamental mechanisms behind the concept between obesity and dengue, however, are rarely discussed. A number of variables, including the existence of cytokines that increase inflammatory response and deregulation of endothelium barrier protein production, contribute to plasma permeability, a defining feature of severe dengue. The key diabetes-related variables that impact endothelium functioning include th-1 skewed responses and the production of junctional-related proteins. Additionally, obesity affects lipid metabolism and the immune system, which increases viral multiplication and inflammatory processes. The common factor among individuals with diabetes and obesity is chronic inflammation, which results in endothelial dysfunction. Explored along with the disease's relationships with diabetes and obesity are the potential causes of comorbidities in severe dengue.

***Keywords*---**dengue virus, cytokines, obesity, diabetes immune system.

Introduction

The dengue virus belongs to the family Flaviviridae within the genus Flavivirus. Flavivirus comprises the most significant group of arthropod-communicated infections, including significant human microbes like dengue, Zika, yellow fever, and West Nile infections (1). Dengue virus contains (+ssRNA) positive-sense single-stranded RNA. The length of RNA is 11 kb and is enclosed by an envelope (2). This virus consists of a single reading frame that is responsible for the synthesis of three structural and is marked by a high fever, sore muscles, a bad headache, feeling sick, throwing up, and a rash on the skin. In dengue cases, bone-break fever is a common symptom. In severe cases, bleeding comes from the nose, and mouth due to blood vessel bursts (3). This infection reduces platelet count. In the case of dengue shock syndrome, frequent vomiting, heavy bleeding,

and sudden blood pressure levels decrease. The symptoms of dengue hemorrhagic fever and dengue shock syndrome lead to death (4).

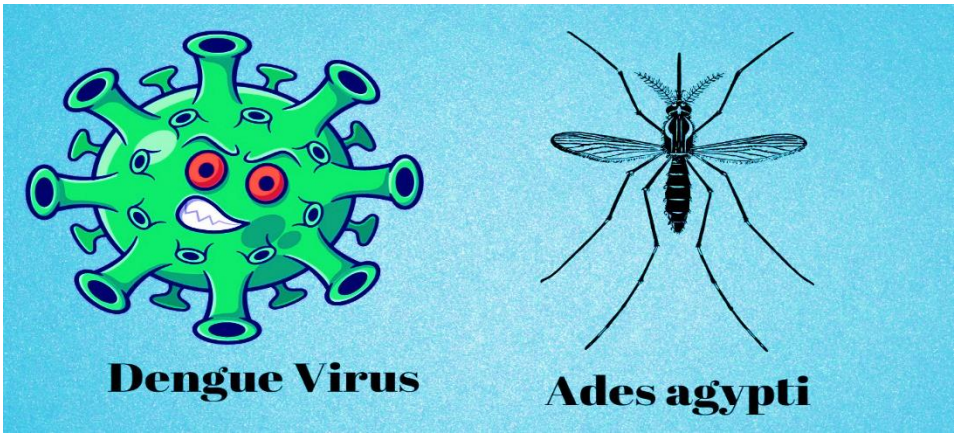

Figure 1: Causative agent and vector for Dengue virus

Dengue virus immunology in the host

The dengue virus enters the body during blood feeding, which is necessary for egg production and spreads through the bite of an infected mosquito (5). The infection is directly infused into the dermis along with salivary fluid, but some experts believe that the cutaneous proclamation also occurs, which may result in direct immunization into the circulatory system. Several other variables are also present at the vaccination site, including salivary components that are known to reduce macrophage penetration at the injection site. This may be due to lower levels of CXCL2 and IL-1 at the bite site, which has the effect of triggering natural immune cytokine replies. The mosquito species CLIPA3 secretory polypeptide (6).

Aedes aegypti has become involved in accessing the intracellular matrix for cell mobility and coupling dengue viral particles to surface receptors on cells. Several cells, including Langerhans cells, progenitor cells, neutrophils, keratinocytes, and fibroblasts, acquire contamination throughout this period (7). This occurs via glycosaminoglycans such as (heparin sulphate, TIM-1, Hat, CD14, and CD300a) with the dengue virus E protein underlying area III, which has been involved as the most realistic scenario for curtailing the cell passage synapses. Other mechanisms include explicit section receptors such as L-SIGN, DC-SIGN, C-type lectins, the mannose receptor, and glycosaminoglycan such as TIM-1 (8).

Dengue virus will invade other healthy cells as allows us to protect and circulate throughout the bloodstream, eventually leading to virus infection. When the flexible immune reaction is activated with the formation of immunoglobulin, such as immunoglobin (Ig) M and IgG, the infection level in the blood decreases and the individual eventually recovers from Dengue fever. After then, IgM levels start to decline but IgG levels continue to rise (9).

A subsequent dengue viral infection with a different serotype tends to worsen Severe Dengue with increased itchiness and excessive cytokine production (10).

It's possible that earlier IgG antibodies didn't completely eradicate the pathogen, but rather helped cells with the Fc receptor become resistant. The term "counteracting agent subordinate upgrade" refers to this peculiarity. High Dengue virus antibody titer and a cytokines cascade will result from this, which will ultimately cause Seagate migration (11).

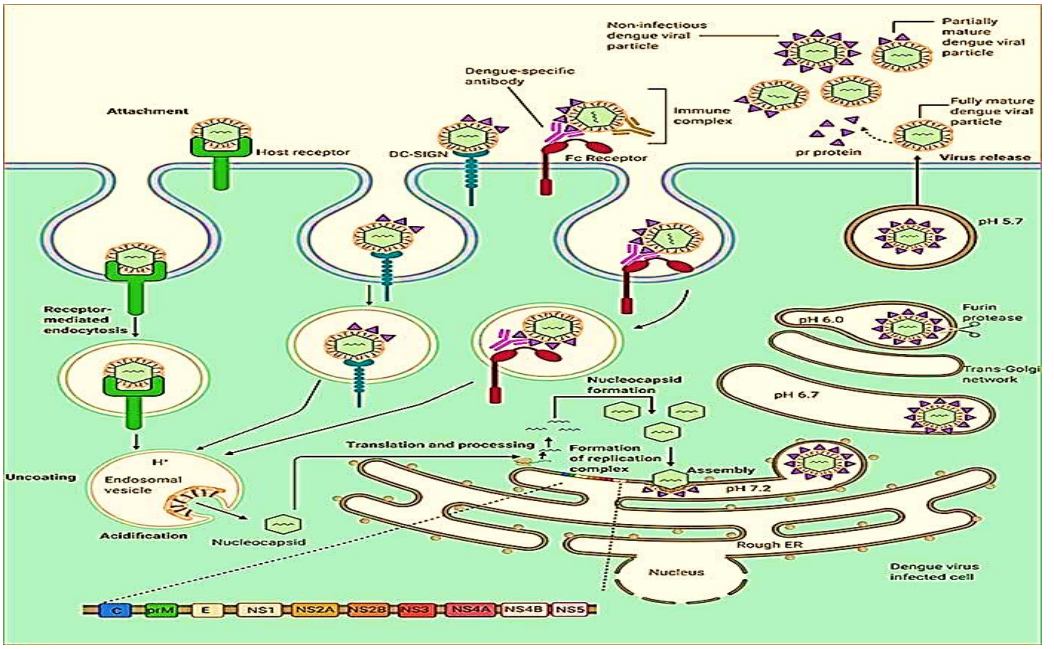

Figure 2: Life cycle of Dengue virus in a host body

Immunopathogenesis of Dengue viral infection

T-helper cells play a big role in inflammation and the adaptable immune system. There are two main types of T-helper cells, and they are (T-helper type 1 cell and T-helper type 2 cells) (12). Most people are aware that the identification of the production of cytokines can be used to distinguish between different types of T-helper cells. Interleukin-2 (IL-2) and interferon (IFN-) are produced by T-helper type 1 cells while IL-4, IL-5, IL-9, IL-10, and IL-13 are produced by Th-2 cells (13). Some of these cytokines are also involved in the polarization of T-helper cells and in maintaining the balance between T-helper type 1 cell and T-helper type 2 cell replies. The precursor to T-helper cells, Th-0, also known as a guileless lymphocyte, is capable of dividing into (T-helper type 1 cell and T-helper type 2 cells) under clear circumstances during immune system pathogen preparation (14).

The two main mediators that control the transition of Th-0 cells to T-helper type 1 cell are IFN- and IL-12. T-helper type 1 cell can activate macrophages by releasing IFN-. These activated macrophages, also known as M-1 macrophages, pull in lymphocytes, natural killer cells, and neutrophils to assist inflammatory responses (15). The initial stages of the T-helper type 1 cell response are triggered by the delivery of IL-12 and IFN- by antigen-introducing cells and regular executioner cells. The activation of Stat-4 and Stat-1 as signal transducers and

activators of record factors through the separate utilisation of IL-12 and IFN- ultimately triggers T-bet articulating due to the enlarged accessibility to TBX-21 promotional location (16).

As a result, the integrity of IFN-γ is effectively transmitted and IFN-γ is produced in greater quantities. Additionally, the activation of T-bet quality and the availability of IFN- prevent IL-4 from being released, preventing the transition to T-helper type 2 cells. Stat-5 and Gata-3 must be activated for T0 to transition to Th-2, and IL-2 appears to be the least potent cytokines to do so when compared to (IL-4, IL-7, IL-9, and IL-15) (17). However, IL-4 starts stat-6, which eventually extends GATA-3 (a GATA-limiting peptide articulation). Stat-4 is downregulated as a result, preventing the Th-1 differentiation from emerging. Because of their soothing effects, IL-4 and IL-10 produced by T-helper type 2 cells are renowned for reducing the severity of a variety of infections, including immune response encephalomyelitis and joint inflammation arthritis (18). Additionally, linked to tissue repair and preventing the production of T-helper type 2 cells related protein, IL-4 and IL-13 released by T-helper type 2 cells delay twisted healing in vivo. For example, Behcet's disease, Crohn's disease, and multiple sclerosis can have poor clinical outcomes due to an imbalance of T-helper type 1 cell and T-helper type 2 cells cytokines; as a result, the T-helper type 1 cells and T-helper type 2 ratio should be taken into account to improve inflammatory disorders (19).

IFN- γ and TNF- are T-helper type 1 cell's Proinflammatory cytokines responsible for a variety of processes, including damage to the endothelium and the vasculature. Numerous studies have demonstrated a correlation between higher IFN- γ and TNF levels and the severity of dengue (20). In vitro endothelium damage caused by this mixture is mitigated by the NO channel. This was also looked into, and it was discovered that using NO foragers and NO synthesize inhibitors prevented the endothelium damage caused by these cytokines. However, another in vitro investigation found that IFN-γ accelerated endothelial cell death, possibly as a result of a reduction in nitric oxide production. In endothelial cells, NO is recognized for its protective role and prevents apoptosis in response to a variety of threats, including UVA, tobacco smoke intensity, cadmium, and ICAM-interceded leukocyte clutch (21).

Despite this, high levels of nitric oxide may cause apoptotic cell death because they can lead to the formation of peroxy-nitrites when an organism replies with superoxides (22). By increasing the quantity of intracellular Ca2+ and possibly inducing death through the activation of caspases-8 and caspase-9, peroxy-nitrate disturbs the proportion of Ca2+ in the endoplasmic reticulum (23). Additionally, through the phosphoinositide 3-kinase pathway, NO and peroxy-nitrate trigger the grouping of neutrophils external percussion (24). DNA from neutrophils, histone modifications, and other proteins help compensate for neutrophils' external percussion. In a murine model, a recent study found that reducing neutrophil's external percussion with DNase I reduces vascular penetrability (25). A component of neutrophil's external percussion called citrullinated histone-3 disrupts the microvascular endothelial barrier by lowering the adhesion overlap proteins without damaging the cells (26).

The continued research on how neutrophils' external percussion affects vascular porousness is generally too hazy to develop a clear framework. When exposed to neutrophil's external percussion, endothelial cells increase VCAM-1 and ICAM-1 articulation (27). A recent clinical analysis revealed higher levels of neutrophils external percussion in dengue patients, which may contribute to the pathophysiology of the disease. This suggests that neutrophil's external percussion may increase vascular penetrability in endothelial cells and also cause endothelial activation, which in turn causes inflammation and capillary spilling in patients diagnosed (28).

Specifically, in Type 1 diabetes mellitus, the distinct subgroups of T helper cells and their unique cytokines are involved in hyperglycemia. Evidence has accumulated showing that Type-1 diabetes, in particular, has a changed T-helper type 1 cell and T-helper type 2 equilibrium. However, different experts have different opinions on whether T-helper type 1 and T-helper type 2 cells were involved in the intervention (29).

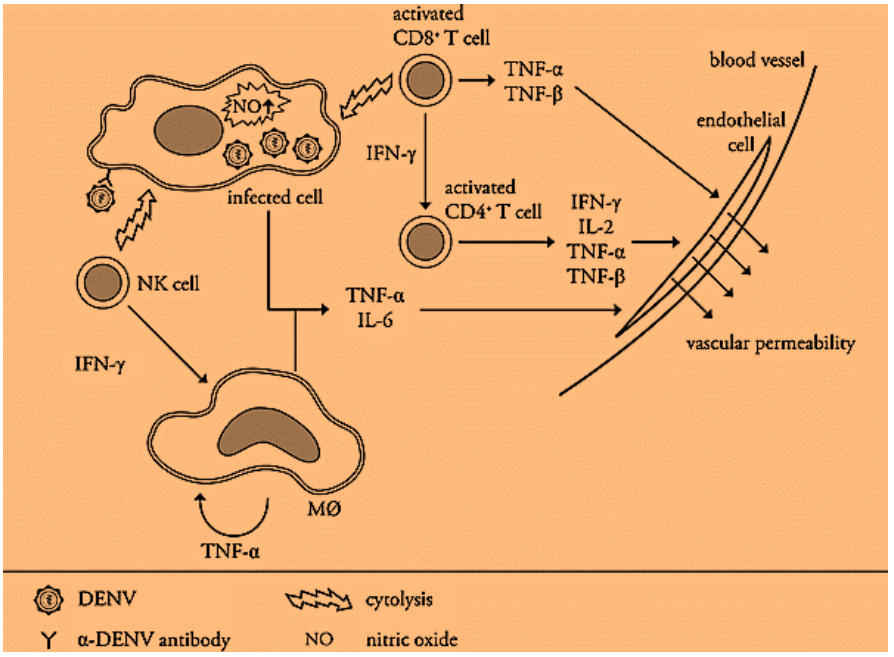

Figure 3: Immunopathogenesis of severe dengue infection

Sami et al concentrations have demonstrated that T-helper type 1 cell and T-helper type 2 cytokines work together to promote b-cell obliteration, which ultimately results in hyperglycemia. The precise cause is yet not fully understood. It is established that Type 1 diabetes is linked to a dysregulated safe reaction, both humoral and cellular and that a switch to T-helper type 1 cell prefers the pathological approach. Furthermore, it is claimed that IL-2 and IFN- γ destroy beta cells by assisting in the recruitment of autoreactive immune response to pancreatic β - cells. Additionally, it is claimed that T-helper type 2 cell production of 1L-10, in particular, accelerated obliteration by facilitating the invasion of these autoreactive cells. However, the specifics of how these two types of helper cells

damage the body vary, and as a result, both T-helper type 1 cells and T-helper type 2 cells, and their roles, participate in and work together to produce pancreas islet-cell destruction in Insulin-dependent diabetes (30).

Protected cells' commitment and role in obesity, particularly in fat tissue, is still not well-established. Fundamentally, fat tissue is made up of a variety of fundamental, metabolism, and secure cells. These spread via a network of intercellular cytokines that originate from various immune cells. The existence of the cells and the associated arbiters is considered to have detrimental effects on our understanding of fat tissue. Adipocytes in the fat tissue are exposed to a variety of factors, including cytokines, metabolites, chemicals, and even toxins, which affect their metabolism capacity and cell abilities. The main cytokines include IL-1, which appears to promote exacerbation and metabolism in human adipose tissue and is obtained from macrophages rather than immune system pathogens (31).

Annoyance is triggered by the presence of presumed resistant cells, which increases the production of chemokines and, in turn, attracts more resistant cells. The robotic functions of Interleukin-1 and Th17 cytokines are still not completely understood. IL-6 and TNF-, which are not produced by immune system microorganisms but rather by CD45 + cells of the fat tissue cells, are two of the several factors likely adversaries provided by the fat tissues. In any case, their vitality is still fluctuating. Relating other Th-1, a different study found that adipocyte-determined leptin promoted the proliferation and segregation of CD4+ Lymphocytes to Th1 cells in mice, resulting in enlarged Th-1 cells that triggered resistance-associated irritation and IFN-γ production disproportionately. This accelerated the M1 aggregation of fat tissue macrophages, which led to the release of cytokine production that irritated the body and blocked insulin action (32).

Endothelial breakdown is a common phenomenon in some non-transmittable diseases, such as diabetes and obesity, which may increase the risk of progression to severe dengue infection. This is probably due to endothelial breakdown affecting the distinctive adhesion of hosts who have lately been exposed to some other serogroup, which then permits fluid shift to ensue. A non-transmittable disease problem is also growing, and within this group, diabetes mellitus is emerging, affecting 478 million patients worldwide (33). Observational studies identified diabetes mellitus as a risk factor for severe disease and suggested that it may be the underlying problem that exacerbates the dengue-related clinical problem and leads to discomfort. Diabetes mellitus affects the endothelium's physical and physiological integrity because it causes an ignitable situation due to lymphocyte activation, which triggers the arrival of cytokines that are conducive to fire. A comparable situation is found in obese children who have a higher risk of contracting dengue infections and present with extra unexpected symptoms including encephalopathy and fluid excess (34).

Comorbidities associated with obese people with dengue viral infection

Despite current therapies, this peculiar lipid environment is linked to vascular complications in diabetes. The Base 40% wage group is constantly looking for methods to increase their income, thus they ignore their health issues like

diabetes and obesity and thereby increase their risk of developing a serious dengue infection. According to a Brazilian study, the risk of dying from dengue is ten times greater in individuals who have undiagnosed normal comorbidities and much higher when multiple comorbidities are present (35).

In their analysis of comorbidities such as diabetes, irresistible illness, pneumonic infection, and renal disease were identified in a significant portion of dengue deaths. To achieve WHO's goal of a 50% decline in dengue-related mortality and a 25% reduction in devastation by 2020, persons with comorbidities must be precisely admitted to dengue safety measures (especially quick clinical examination). One further study in Pakistan found no true correlation between dengue and either dengue hemorrhagic fever or dengue shock disorder, even when researchers included selected comorbidities such as diabetes mellitus, hypertension, bronchiolitis, chronic lung disease, and chronic liver diseases (36).

Obesity: a possible risk factor for severe dengue

On World Diabetes Day, numerous initiatives were finished to raise awareness of the effects of diabetes. According to the Public Diabetes Vault Report, Malaysia's adult diabetes patients in 2020 had hypertension and dyslipidemia, respectively, in 80.0% and 75.7% of cases. In Asia, Malaysia has the highest percentage of obese and overweight people, and up to 7 out of 10 adults suffer from chronic illness. Insulin blockage caused by obesity is a major risk factor for type 2 diabetes and cardiovascular disease. Numerous endocrine, provocation, brain, and cell-specific pathways are dysregulated in obesity. However, it's possible that these factors are connected and that a specific transaction underlying the pathophysiology of insulin resistance (37).

Repulsiveness is frequently linked to an increased risk of a variety of chronic conditions, including diabetes, dyslipidemia, poor emotional health, impacts on the risk of stroke and cardiovascular disease, certain cancers, and osteoarthritis (38). The effects of a global obesity epidemic may also increase the prevalence of irresistible diseases that are linked to obesity, hence irresistible disease awareness is anticipated in populations with high levels of overweight/stoutness. Therefore, it is necessary to have better clinical practice guidelines for obese persons. Understanding these many physiological systems will enable suitable interventions that specifically prevent or treat insulin resistance and its associated diseases (39).

In addition to affecting the patient's vital organs, these ailments can also harm their metabolism, which can damage their capillaries. Vascular entanglements continue to be linked to a peculiar lipid environment (40). Also claimed is the sensitivity of the mediator metabolic pathway of again lipogenesis to insulin. The fact that this mechanism effectively combines lipids from simple precursors could add to these complexities. Again, unsaturated fat synthase is necessary for lipogenesis, and it has been suggested that endogenously produced lipids affect the endothelium's function (41).

Risk factors and Biomarkers of dengue in obese peoples

In general, obese individuals exhibit higher degrees of annoyance coupled with endothelium damage. Recently, there have been more research publications demonstrating a connection between obesity and dengue (42). The system that supports the involvement of these 2 factors (being fatty and diabetic) in dengue patients, however, just addresses a probable affiliation. According to a meta-analysis published in 2018, pediatric kids' weight acts as a risk factor and is associated with severe dengue. Further, recent research objectives have shown that obese people have devastating clinical symptoms and greater dengue severity (43).

In another study linking obesity to acceptable breakage, Afroze et al. remarked that obese persons are more susceptible to several diseases. In his studies, he demonstrated that leptin regulates the flexible immune system by adjusting the safe balance in obese individuals and promoting macrophage phagocytosis by increasing the emission of pro-inflammatory cytokines. This weakens the protective barrier and increases the risk of postoperative, nosocomial, respiratory, hepatobiliary, gastrointestinal, and periodontal infections. Hyperleptinemic individuals are also thought to be corpulent, and this correlates with a weakened immune system. Despite the increased prevalence of both obesity and Dengue virus infections, there is still a lack of information directly linking obesity and dengue (44).

Inflammatory cytokines and immune-related metabolites, but not viral NS1 protein, with disease severity of dengue virus infection

Another study by Tsheten et al. revealed various clinical and research center findings, including higher rates of hemoconcentration relapse, severe thrombocytopenia, increases in creatinine and liver compounds, and warning signs of increasing hematocrit with rapid platelet loss and longer duration of hospital stays, which were demonstrated to result in more significant illness seriousness associated with dengue virus diseases among fat patients. Additionally, this necessitates more caution when interacting with this group of patients (45). ICAM-1, an intercellular bond particle, is aberrantly conveyed at low levels in endothelial cells and plays a key role in controlling the grasp of the cells. ICAM-1 has been detected at higher levels in both animal models and humans. Mice that consume a lot of fat have large levels of ICAM-1 in their blood plasma, which may have been produced by the fat tissue. When compared to typical muscle or fat synthesis folks, healthy control large people have higher serum levels of cell bond atoms. High ICAM-1 articulating can disrupt grip contacts, obstruct endothelial cell function, and produce irritation. The MAP-K pathway controls ICAM-1 in cerebral and microvascular endothelial cells. ICAM-1 feeling increases TNF-mRNA half-life and triggers other flammable cytokines (46).

ICAM-1 overexpression results in an actin cytoskeleton disruption and a lack of endothelium blockage integrity. Strangely, ICAM-1 activates JNK, which causes VE-cadherin to bind and act as a provocative biomarker as well as prevent polymorph nuclear neutrophils from migrating. High levels of ICAM-1 may result in increased solute penetration through venue endothelial cell surfaces, while low

levels of leukocyte appearances may result in low levels of ICAM-1 (47). Even in the presence of TNF-, the effects on solute permeability are drastically diminished without leucocyte-endothelial cell collaboration (48). The claim is that ICAM-1 increases unquestionably in pro-inflammatory conditions. Studies suggested that viruses interfere with lipid amalgamation and digestion in their replication cycles by taking advantage of the creation of the twofold layer vesicles during autophagy for effective replication. Metabolomics focuses on using quadrupole season of-flight fluid chromatography coupled mass spectrometry (QTOF-LCMS), which revealed that metabolites delivered in DWOWS, DWWS, and patients worked with the lipid digestion pathway (49). A considerable amount of the metabolites in DWOWS patients are thought to be involved in the digestion of unsaturated fats for energy and the production of fatty oils, phospholipids, and other important layer elements to maintain cell cycles and repair damage caused by DENV illness. However, patients with severe dengue and DWWS transmitted a large number of metabolites related to the phospholipid digestion pathway, which regulates growth (50).

Dengue virus-induced autophagy regulates lipid metabolism

Phospholipids are a group of lipids made up of phosphate groups that have the potential to frame lipid bilayers and function as important components of cell membranes. Differentially communicated in dengue patients, especially those with severe dengue, were components from various classes of phospholipids, such as phosphatidylcholine, phosphatidylglycerol, and phosphatidylserine as well as phosphatidic corrosive, which are precursors for other more complicated phospholipids (51). The progressions in exogenous admission of unsaturated fat from the patient's diet during illness or the modified activities of lipid-using enzymes suggested by the dengue virus are likely to be the causes of liberated phospholipid digesting (52). During a dengue virus infection, layer penetrability may become unstable due to alterations in phospholipid digestion. Additionally, in individuals with severe dengue, compounds from the sphingolipid digestion pathway were explicitly reported. Sphingolipids are primarily found in the layers of the brain and sensory cells, and when they are altered, they can result in the revision of film segments associated with various neurological diseases. The connection between this and the unusual neurological disorders, like brachial neuropathy or encephalopathy, that are observed in individuals with severe dengue, may then be made (53).

Immunomodulation in obese people infected with dengue

Considering the known biochemical interconnections between adipocytes and the immune system, it may not be remarkable that obesity has been found to change the immune system, specifically immunomodulation, in many ways. Some of these alterations include adjustments to NK cell activation, CD8+ T-memory cell generation, T-cell metabolism, and antibody repertoires. With a few important characteristics separating them, obesity and ageing have antibody response attenuation levels that are identical. First and foremost, obese individuals have a reduced number of reducing B-cells while also having higher levels of enhancing flammable B-cells. Total B-cell activity is also compromised by decreased AID function (54).

This appears to be caused by the increased production of pro-inflammatory cytokines by activated B-cells, including intracellular TNF, which all have a negative correlation with AID activity as a result of AMPK's upstream regulation (55). This fact could influence Dengue virus infection in two key ways. It has already been established that it seems likely that the creation of more proinflammatory antibodies will lead to tissue damage and endothelial dysfunction. The much more fascinating idea is that this mechanism could also affect antibody-dependent enhancement, leading to a more serious illness. Obese individuals may have decreased B-cell activity, which could lower protective antibody titers, raise the possibility of antibody-dependent acceleration, and raise the possibility of Severe Dengue occurrence (56).

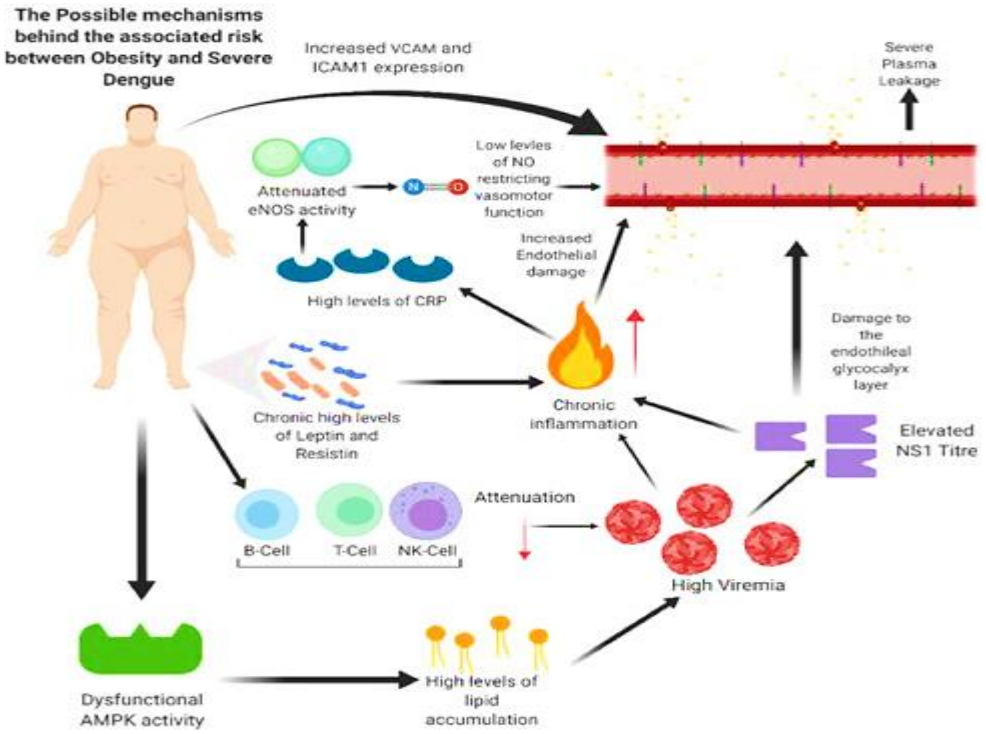

Figure 4: Physio-pathological mechanisms of Dengue virus in obesity (38)

Obesity also leads to an increase in inflammatory monocytes, as shown by an increase in (CD16+) circulating monocytes in humans and an increase in the accumulation of M1-activated macrophages in adipose tissues. It is well known that the dengue virus main target cells are monocytes and macrophages. Provocative monocyte and macrophage subsets, however, are more susceptible to dengue virus infection and trigger more significant proinflammatory responses, such as IL-1, TNF-a, IL6, IL-18, and CCL2, 3 and 4, which may enhance illness severity. Therefore, the systemic low-grade chronic inflammatory state associated with obesity may hasten severe dengue progression by enhancing proinflammatory reactions to the dengue virus (57), (58).

Obesity has been demonstrated to have a major impact on T-cell metabolic function, and repertoire. Obese people have been reported to have fewer T cells

overall, and those that are present have diminished functioning, such as lowered IL-2 receptor expression and INF-γ production (59). An increase in pro-inflammatory T cell subtypes, such as Th-1, Th-17, and CTLs, which are cytotoxic T lymphocytes, is another effect of high leptin levels. These processes may intensify an already heightened T cell response seen during severe dengue, leading to T cell death of dengue-specific T cells and the failure to eradicate virus-infected cells (60).

Obesity affects the development and metabolism of T-cells. As an important factor in T-cell differentiation function, and cytokine secretion, metabolic processes have an impact on the establishment of diverse subsets of T-cells during infections. The constriction of antigen-specific T-cell populations and the production of persistent memory T-cells after the peak of the effector response are also supported by modifications in metabolism (61). As a result, metabolic dysregulation in obese people is expected to have an impact on memory T-cell survival and the antiviral activities of the T-cell response during dengue infection. Obese adults and children exhibit altered T-cell and antibody responses to influenza vaccination. Additionally, compared to their leaner counterparts, weighty mice exhibit a decreased immune system microbe response to elective flu disease infection, which increases the risk of infection (62).

Additionally, investigations show that obese people have weakened immune reactions to tetanus, hepatitis-A, herpes, and hepatitis-B immunizations. T-cell proliferation declines as a result of an infection, which reduces the immunological mechanism. This could indicate that obese people undergo a pro-inflammatory activity that lasts longer during the dengue virus because it takes longer to eradicate the virus and activate the immune system. Excessive activation of T-cells with suboptimal effector capabilities and a deficiency of essential antiviral T-cell subtypes, such as T-cells, may result from this. As a result, the infection sites sustain more harm over a prolonged period (63), (64).

Natural Killer cells, which are crucial elements of any antiviral activity in the initial stages of infection, are also known to be impacted by obesity (65). It has been shown that prolonged exposure to leptin, which is present in obese people, impairs both the immune system function of Natural Killer cells and the proliferation of Natural Killer cells, even though transient openness to leptin has been shown to promote the formation between Natural Killer cells and cancer cells as well as a higher articulation of TNF-related apoptosis instigating ligand. Obese children's Natural Killer cells were discovered to be metabolically strained and cytotoxically compromised in comparison to their non-obese peers (66).

According to a new study, the metabolic paralysis brought on by environmental lipid intake affects the NK cells' capacity to kill cancer cells in obese people. Because of the drastically decreased function of NK cells in obese people, the immune system's capacity to stop the spread of DENV during early infection would be severely impaired (67). Additionally, research on mice suggests that NK cells function as rheostats, controlling the antiviral T-cell activation and that NK cell dysfunction is linked to an elevated CD8+ T-cell response in hepatitis B infection. These results imply that NK cells directly destroy antiviral CD8+ T-cells

or eliminate virus-infected cells to modulate the immune response of CD8+ T-cells (68).

Conclusion and future prospective

It has been proposed that pre-existing sensitivity to the Dengue virus can either reduce or worsen a severe infection using antibody-dependent activation. Understanding how human immune systems, which include antibodies, T-cells, cytokines, and a host of other components, balance preservation against pathophysiology is crucial given that the Dengue virus has emerged as a major worldwide health concern. However, it is still unclear how these numerous components, including those connected to the host and viruses, interact with cells and molecules. Obesity and diabetes both appear to share a biological mechanism that raises the likelihood of developing severe disease, and endothelial dysfunction. This most likely happens by making the endothelium surfaces of hosts who have already been infected by one serotype more permeable, allowing for a fluid shift to happen. Severe dengue is characterized by vascular leakage.

Diabetes is a standalone risk factor for severe dengue because it changes the structural and physiological integrity of the endothelium as a result of a chronic inflammatory condition brought on by lymphocyte activation that releases proinflammatory cytokines. The same process occurs in obese kids, who have a higher risk of getting dengue viruses and exhibit more odd symptoms including encephalopathy and fluid excess. Due to this aberrant lipid environment, obesity is linked to vascular problems despite the efficiency of current treatments. The molecular mechanism by which diabetes and obesity increase the risk of developing dengue hemorrhagic fever may be endothelial impairment. People with lesser wages often disregard their health problems like being overweight and obese to increase their money, which increases their risk of developing severe dengue. It's also conceivable that many obese and diabetic individuals contract dengue for the first time in a subclinical or asymptomatic state, and that recurrent infections with various serotypes may result in greater inflammatory reactions on the endothelium.

We are interested in knowing how these individuals would be able to see the logically rising incidence of severe dengue in these categories of persons with fundamental comorbidities. To restore normal endothelial responses in these areas, extra care must be taken. The lack of access to appropriate human sample collection and an effective infection model has stymied this advancement in our understanding of the mechanisms underlying the dysfunctional endothelium, which is especially important for the development of vaccines. People with the disease respond differently around the world, which is especially crucial to understand for therapeutic applications.

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